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REVIEW

The Erosion of Healthcare and Scientific Integrity: A Growing Concern

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Background: Tremendous achievements in healthcare and science over the past 200 years have enhanced life expectancy in parallel with a shift from dogma to humanistic liberal education. Advancements in cancer have included vaccines treating causes of cancer (eg, hepatitis C-induced liver cancer and human papillomavirus-induced cervical cancer) along with improved cancer survival in children. In contrast, developments in cancer, frequently touted as "discoveries" or "breakthroughs" in media headlines, have been demonstrated to be ephemeral rather than game changers. In reality, cancer incidences are increasing, and relapse and mortality rates have not changed substantially. By this, we are experiencing today similar challenges to those before the so-called Humboldt reform. The trend towards managerialism with a focus on quantity in health care and science endangers their integrity.

Methods: Due to the complexity of integrity of healthcare and science, in-depth contemplation of this review contains foundations of actions in healthcare and science, information regarding cancer, as an example, quantity focus of healthcare, technology, publishing, marketing and media, predatory publishers, followed by psychologic and sociologic aspects which influence our perception.

Results: A complex paradoxical transformation has occurred, in which quality and humanism have been replaced by quantity, revenue, and marketing, together with "citation silence", (ignoring original findings), and increased corruption and misconduct. This shift explains why the integrity of healthcare and science is being eroded.

Conclusion: Countries and societies are only as strong as their healthcare and science, both of which are only as strong as their emphasis on quality and integrity. Awareness of this situation may represent a first step toward a renewed focus on accountability.

Keywords: healthcare, science, integrity, quality, quantity, accountability

Introduction

Healthcare and Science Gains

Healthcare and science have made tremendous gains in the past 200 years, notably with respect to life expectancy, largely because of decreased infant mortality and the introduction of antibiotics, thus limiting the damage caused by infectious diseases.[1] For decades, outcome improvements were based on discoveries in hygiene, microbiology, workplace safety, and standardization of diagnosis and therapies.[2]

Another reason for the success in recent centuries was that the Enlightenment led to an intellectual awakening with a focus on reasoning and logical explanation. Current cancer therapies still are based largely on treating symptoms rather than the underlying causes. Achievements in preventing cancers arose from using vaccines to treat the causes of pathogen-induced cancers, for example in hepatitis C and hepatocellular carcinoma, or in human papilloma virus and cervical cancer.[3,4] Other notable achievements were made in pediatric cancers; currently, nearly 80% of children with cancer survive, whereas fewer than 10% survived in the 1950s.[5]

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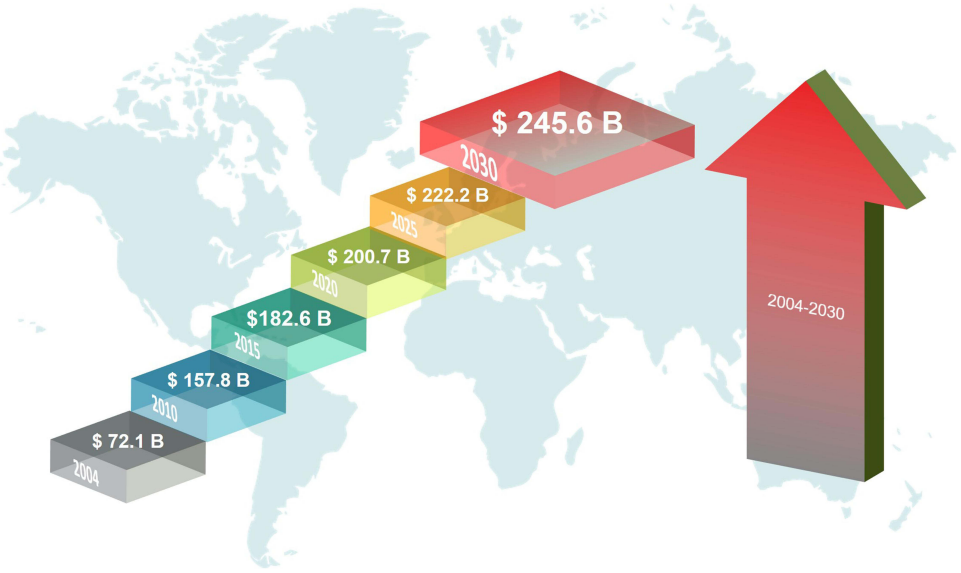
Graphical Abstract



Cancer Epidemiology

The incidence of cancer occurs at rates of 49.2% in Asia, 22.4% in Europe, and 13.4% in the U.S./Canada.[6] The global population is estimated to increase from approximately 8 billion in 2022 to 9.7 billion in 2050, and more than 35 million new cancer cases are predicted to occur (77% increase).[7,8]

The incidence of colorectal, breast, lung, and prostate cancers is likely to double by 2070.[9] An estimated 30% increase in pancreatic cancer prevalence by 2040 has been predicted.[10] Not only in developed countries[11] but also in developing countries, colorectal cancer (CRC) incidence in young adults 20–49 years of age is rising at alarming rates.[12–14] Although survival benefits have been achieved in some subpopulations, overall cancer mortality has not substantially decreased.[6,15] CRC relapse rates decreased by 4.7% between 2004 and 2019, only with inclusion of a period between cancer surgery and recurrence, depending on the stage of the disease,[16] thus indicating achievement of only marginal improvements with better follow-up and screening protocols. Overall, CRC recurrence rates remain high (as much as 40%)[17] In breast cancer, the recurrence rate is approximately 60%,[18] and that in pancreatic cancer exceeds 70%.[19]

Likewise, recent trends in mortality rates and life expectancy have decelerated since 1990.[20] Interestingly, health expenditure is not the only variable influencing lifespan or health span; therefore, financial input is only one of many factors influencing health outcomes (Figure 1).[21] Visualization helps delineate issues but is not sufficient for understanding causality. A prediction made by Erwin Chargaff (1905–2002)—"Cancer has been cured for decades now with the result that it is increasing"—unexpectedly remains a reality.[22]

The integrity of healthcare and science is at risk, and awareness of these issues may serve as a step toward a renewed focus on accountability in research. By this, we are experiencing today similar challenges to those before the so-called Humboldt reform. The trend towards managerialism with a focus on quantity in health care and science endangers their integrity.

Methods

Due to the complexity of integrity of healthcare and science, in-depth contemplation contains the foundations of actions in healthcare and science, information regarding cancer, as an example, quantity focus of healthcare, technology, publishing, marketing and media, predatory publishers, followed by psychologic and sociologic aspects which influence our perception. Here, the evolution of healthcare and cancer research and cancer outcomes have been examined over the past two centuries. A wide-ranging scope review covered many disciplines synthesizing and generating a new perspective

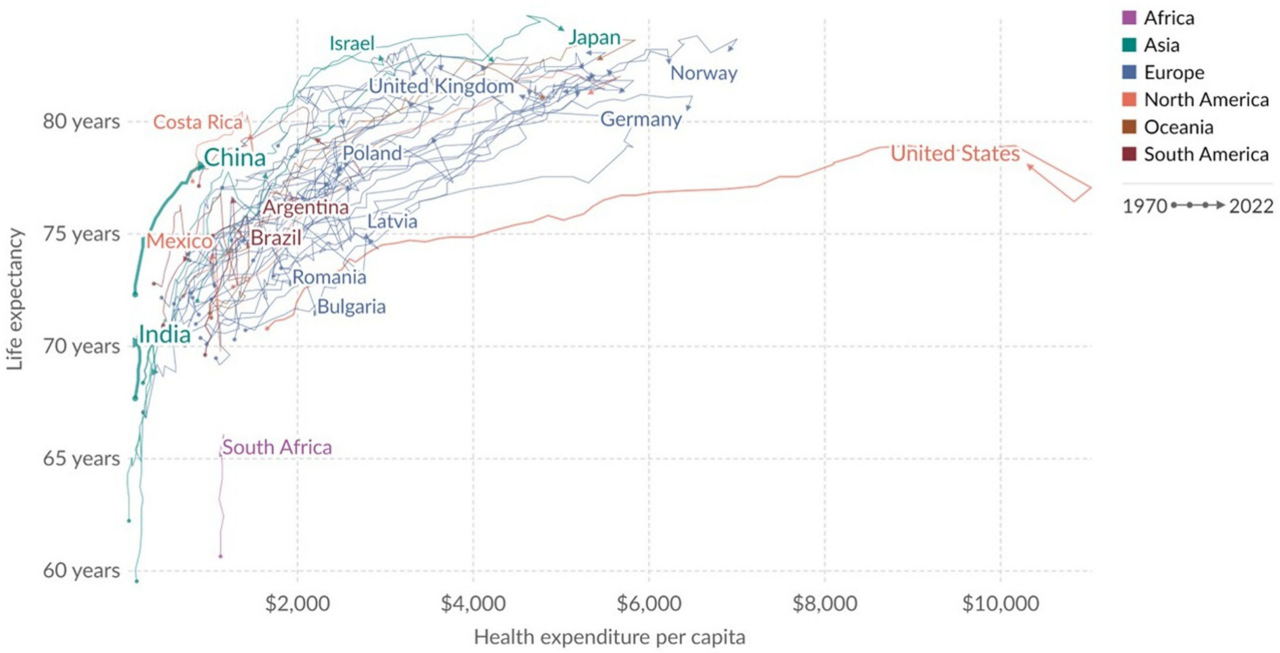


Figure 1 Life expectancy vs health expenditure, 1970 to 2022. Health expenditure data are expressed in dollars at 2015 prices, and the data are adjusted for inflation and differences in cost of living between countries. Data source: UN, World Population Prospects (2024); OECD Health Expenditure and Financing Database (2023). Graph Accessed from Our World in Data, Oct 27, 2024. Available from: https://ourworldindata.org/grapher/health-expenditure-and-financing-per-capita. Creative Commons.[21]

to identify key findings with research gaps. The literature cited helps explain why we are where we are today. There is hope that engenders further debate on how we can move forward with better healthcare outcomes.

Foundation of Actions

A foundation for actions to obtain the best outcomes is the aim of healthcare and science. The inscription at the Allgemeines Krankenhaus in Vienna, Austria, since 1834, "Saluti et solatio aegrorum" ("For the salvation and solace of the sick"), describes the aims of healthcare. The Hippocratic philosophy on which Western medicine is based is an Ionian natural philosophy that distanced itself from religious-magical ideas and indicated that diseases are caused by natural factors. Nevertheless, the four-humor doctrine was a fallacy, and Hippocratic-Galenic medicine shaped medical practice for almost 2000 years. As a relic of the Middle Ages, constructing, interpreting, and imposing it on others as a mandate from heaven was commonplace. In parallel, since the 16th century, an intellectual awakening, known as the Enlightenment, led to the replacement of ideology with humanistic education, first in Italy, and later in France, Germany, and the United Kingdom.[23] The principles of Humanism were non-religious and ethical, embracing rationality and rejecting supernatural forces, and engaging in healthy skepticism and lifelong learning, to better understand the world through a much more scientific approach. Natural science is based on observation and experiments, and contains the branches of physics, astronomy, chemistry, Earth science, and biology. However, believers of most faiths usually perceive any other representations as blasphemy and a declaration of war against religion.[24]

The aim of science is knowledge. Being curious, asking questions, re-questioning, verifying, and testing to advance knowledge (science) are fundamental to gaining insights. Attempts to find answers have no safety net, and may lead to failure or to knowledge, both of which characterize science. To doubt, remain neutral, value-free, objective, transparent, verifiable, and reliable, and to apply critical thinking, are mandatory aspects of scientific reasoning. This process applies to "detached objectivity", or preferably "objectivity at a distance", and is crucial to scientific progress.

More detailed information regarding cancer, as an example, may inform further discussions.

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Cancer

Majority of Cancers

Most cancers (80.5%) are epithelial (Table 1),[6,25] whereas a minority (10%) are mesenchymal (eg, sarcoma, myeloma, and leukemia) tumors, lymphatic system tumors (eg, lymphoma and myeloma), central nervous system tumors, meningiomas, and mesotheliomas; the remainder form a highly heterogeneous group of other malignancies.

Only 4 of 12 assessed cancer sites (CRC, esophageal, lung, and oral) have shown any gains in the survival of patients with distant metastatic disease at diagnosis.[26] Intriguingly, among Mormons living in Utah, US, the epithelial cancer incidence in 1980 was 50% lower than that in the rest of the country.[27,28] In male members of the Seventh-Day Adventist Church, the rates of colorectal, lung, and bladder cancers, as well as bladder papillomas, were approximately 80% lower than observed in a similar age-matched population.[29] Otherwise, the incidence of gastric cancer in developed countries is nearly 3-fold higher than that in developing countries.[2]

Primary CRC over a 25-year period (1989 to 2014) did not change substantially with respect to historic data,[30] and similar findings have been observed for synchronous metastasized CRC.[31] Significant improvements in median survival in patients with primary CRC and metastasis with more aggressive therapy were achieved from 2010 to 2015,[32] and patients with CRC with liver metastases achieved a 5-year survival of 33%.[33] This survival benefit of metastasized CRC is dependent on the volume and function of the remnant liver;[34] however, knowledge regarding functional liver volume after hepatectomy dates to the time of Klemens Emil Ponfick (1844–1913).[35] Improvements in liver metastases of CRC, and in groups of metastasized cancers of the esophagus, lung, and head and neck, have been observed, thereby resulting in a 3% increase in survival;[26] consequently, these data have not changed substantially and have remained nearly constant for decades.

Improvements in cancer survival with immunotherapies have been encouraging for melanoma[26,36] and new androgen receptor inhibitors in prostate cancer[26,37] Early localized cancers show favorable survival,[26] whereas early cancers with metastasis to lymph nodes often show poor survival. Otherwise, improvements in survival for ovarian or uterine cancers cannot be attributed to immunotherapies, because no new immunotherapies were introduced for these cancers.[26] Metastatic breast cancer survival has not improved substantially over a 30-year period,[38] and similar findings have been observed for metastatic gastric cancers over a 20-year period,[39] whereas marginal improvements have been observed for pancreatic cancer,[40] despite sub-selection of patient groups.

The relapse rate for pancreatic cancer remains at approximately 73%.[41] Approximately 80% of all prostate cancers develop bone metastases within 10 years, even after radical prostatectomy.[42] Furthermore, radical mastectomy or removing occult positive lymph nodes has not increased overall survival.[43] Caesar's quotation from more than 2000 years ago still applies: "People generally like to believe what they want".[44]

Cancer Mortality Over Longer Periods

A more nuanced evaluation of data on the effectiveness of cancer therapies might be achieved by moving from comparing mortality rates over 20-year periods to 80-year periods (Table 2).[45–53] No substantial change in overall cancer unadjusted mortality rates occurred between 1937 and 2022 in Germany or the US.

Table 1 Mass of All Cancers are Epithelial Cancers.

Epithelial Cancer Percentage	Cancer	Number	Percentage
80.5%	Gastrointestinal cancers	5,026,243	26%
	Gyneco-oncologic cancers	3,660,202	19%
	Uro-oncologic cancers	2,529,351	13.1%
	Lung cancers	2,206,771	11.4%
	Epithelial dermato-oncologic cancers	1,198,073	6.2%
	Head and neck cancers	933,931	4.8%

Note: Data from these studies.[6,25]

Table 2 Unadjusted Cancer Mortality in Germany and the US in 1937 and 2022.

Overall Cancer Mortality	1937	2022
Germany	140,000 of 68 million	239,552 of 83.16 million
	0.21%	0.29%
U.S.	136.939 of 128.8 million	602.350 of 331 million
	0.106%	0.182%

Note: Data from these studies[45–53]

Currently, age-adjusted data are frequently used as a health indicator and a means of comparing populations with different age distributions. Furthermore, age-adjusted rates are currently used in a key argument indicating how cancer incidence and mortality rates have improved. This argument is largely as follows:

The pre-pandemic age-adjusted cancer-related mortality rates of both sexes in the US were 198.8 per 100,000 in 2000, compared with 147.8 per 100,000 in 2019.[54] This result was reported as a net improvement in US mortality rates. Of note, the global population in 2000 and 2019 was estimated to be 6.17 billion and 7.81 billion, respectively.[55] Interestingly, the corresponding population data for the US were estimated to be 281.48 million in 2000 and 337.79 million in 2019, or 4.6% and 4.3% of the global population in 2000 and 2019, respectively. Similarly, in Germany, the population was estimated to be 81.8 million in 2000 and 83.56 million in 2019, representing 1.3% of the global population in 2000 (81.8 million of 6.17 billion) and 1.06% in 2019 (83.56 million of 7.81 billion). Given that the overall mortality in both countries did not decrease substantially (Table 2), we are left with the impression of a fundamental survival benefit for cancer patients.

Thus, although age-adjusted data, which are *relative indices for comparison*, are useful for providing information about potential risk, they are too often assumed to be accurate measures of rates, particularly when age structures or groups diverge.[56] This aspect is clearly the case in reporting of statistics on cancer, thereby explaining why the *relative* age-adjusted data are contrary to the *absolute* cancer mortality data, as indicated in Table 2.

Life Expectancy Gain—Cancer Prevention

The US National Cancer Institute (NCI) defines the goal of its prevention program as "the reduction of cancer mortality via reduction in the incidence of cancer".[57] Enormous resources have been invested, beginning with the 1971 War Against Cancer and, since 2016, the Moonshot Program: $1.8 billion was spent between 2017 and 2023 in the US alone. Analogously, a general would be unlikely to send soldiers into battle without knowing the enemy (the cause of cancer), and NASA would be unlikely to send astronauts to the moon without knowing the landing conditions (conditions influencing a cause). Yet most cancers are treated without a known cause, with dismal results. A meta-analysis has estimated life expectancy gains through cancer prevention according to 18 long-term randomized clinical trials in 2.1 million individuals (Table 3),[58] and has reported

Table 3 Estimated Life Expectancy Gain Through Cancer Prevention in 18 Long-Term Randomized Clinical Trials Involving 2.1 Million Individuals.

Screening	Life Expectancy/Days	95% Confidence Interval/Days
Mammography	0	−190 to 237 days
Prostate PSA	37	−37 to 73 days
Coloscopy	37	−146 to 146 days
FOBT	0	−70.7 to 70.7 days
Lung screening	107	−286 to 430 days

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sobering results. However, the preventive effects of such strategies may become apparent later, after several years of randomization, as seen in the NordICC trial.[59,60]

Claimed Game Changers in Cancer

Game changers in cancer are regularly touted in the press, but still overall cancer survival rates of 90% or mortality rates of less than 10% have not been achieved, despite substantial expenditures. Examples of expectations versus reality are presented below.

RNA Breakthrough of the Year, 2002

A total of 80% of RNAs exist for "less than 2 minutes", and approximately 20% exist for 5–20 minutes.[61] Even promoter-independent transcription rates exceed the mRNA half-life. Analysis of blood samples from patients therefore presents a challenge: is the RNA extracted from samples in less than 2 minutes in published studies? Where are the data on RNA extraction times that would allow for objective interpretation of the data?

Cell Division is a "Must" Based on DNA Replication

Without DNA replication, skin cell division in zebrafish occurs as asynthetic fission, and progeny cells have diminished genome sizes and histone levels, and proportionally decreased cell volumes.[62] Therefore, much greater caution is clearly warranted in declaring what is a "must" in nature.

Cell Nuclear Volume Varies According to the Genome Size and Degree of Chromatin Compaction

A long period was required to demonstrate that the osmotic pressure of actively transported proteins determines the cell nucleus-to-cytoplasmic volume ratio.[63] Hence, without measurements of osmotic pressure, data on cell volume and the degree of chromatin compaction are invalid.

Somatic Mutations Cause Most Cancers

Somatic mutations have been searched for "across the whole genomes of 3949 patients with 19 cancer types and 61.2 million somatic mutations".[64] However, in reality, somatic mutations are responsible for only approximately 5–10% of cancers.[65] Even attempts to adapt germline variations as the data of somatic mutations have not been successful; the percentages of, eg, BRCA1/2 or PALB2 for breast cancer were comparable (5.3%).[66] Approximately 7% of patients with cancer for <25 years have been found to carry pathogenic or likely pathogenic germline variants, as compared with 0.09% of controls.[41] Thus, breakthroughs have not been attained for approximately 90% of patients with cancer.

I-Motif Breakthrough

Approximately 53,000 small four-stranded protrusions, called i-motifs,[67] exist in human DNA.[68] In this regard, 99% of bases in the human genome are within 1.7 kb of any ENCODE element, but 95% of bases are within 8 kb of a bound transcription factor motif or DNase I footprint.[69] The functions of i-motifs are also still not understood, so why call this a breakthrough?

Precision Medicine Identifying Genetic Alterations Will Cure Cancer

The NCI-MATCH precision medicine cancer trial had a goal of matching genetic abnormalities in cancer. This approach was suggested to serve as a blueprint for future medical trials.[70] None of the percentage frequencies in the genomic target arms exceeded 3.47%. In approximately 6000 patients with cancer, fewer than 4% showed any genetic correlations with cancer.

Diets Rich in the Antioxidant Resveratrol

Diets rich in the antioxidant resveratrol was reported to slow aging and to be beneficial in many diseases, including cancer. Although a randomized trial burst this bubble,[71] the resveratrol market reached approximately $80 million in 2020, and the revenue is forecasted to reach $116 million by 2028 and $130 million by 2030.

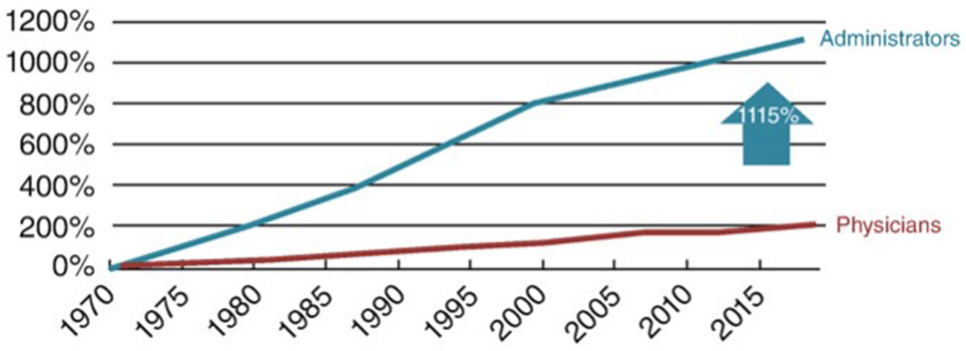

Figure 2 Growth of administrators vs physicians from 1970 to 2017. Graph created by journalist Kevin Drum in 2019, with data from the US Bureau of Labor Statistics.[75] This graph in major modification was also published in Brücher BLDM, Deufert D. German nursing shortage in hospitals – homemade by Profititis. 4 Open. 2019;2:3. Creative Commons.[73]

Liquid Biopsy Detection of Cancer to Prolong Life

Liquid biopsy detection of cancer to prolong life were aimed at detecting as many as 50 types of cancer in early stages, according to the methylation patterns of cell-free DNA. Current test criteria are known to be unsuitable to justify screening programs for saving life.[72]

The commercialization and quantity focus of healthcare, science, and technology continues, whereas the much-vaunted promise of progress remains just a promise, with little to show for the effort.

Quantity Focus

Healthcare

Quality in healthcare and science is assured by those who work in the field.[73,74] The growth rate in healthcare administration between 1970 and 2017 was an astounding 1115% (Figure 2),[75] whereas the growth rate in the number of physicians during the same period was negligible. No evidence indicates that chief executive officers with master of business administration degrees have brought any advantages to healthcare companies. Sales, productivity, investments, and exports have not improved over prior levels,[76] but salaries and the share of salaries to total sales have decreased. No evidence suggests that business administration has led to significant improvements, and only healthcare workers, but not administrators, are benchmarked. Under marketing strategies to increase efficiency and quality through competition, the monetary successful McDonald principle was marketed as integrated care and transferred to hospitals in healthcare (Table 4).

Over a 22-year period in Germany, substantial savings with an increase in treated cases occurred.[73] The cost savings resulted in a performance shift from the hospital sector to the ambulatory sector (rehabilitation centers, nursing homes, and home healthcare) (Figure 3). Decreases in patient length of stay through the diagnosis-related group system resulted in a performance shift from inpatient cases to pre-hospital and post-hospital patient cases without benefit to the patient population. A lack of annual adjustments and consideration of stepwise variables has resulted in a continual increase in funding gaps (Figure 4). Because employees are the greatest company expense, continual savings have resulted (Figure 5), again with no improvements in patient outcomes. The COVID-19 pandemic posed challenges and stresses,[77,78] and brought employees'

Table 4 Transfer McDonald Principle with a Focused Offer, Large Quantity, and Declared Consistent Quality, Plus a Selective Increase in Products in Health Care and Hospitals

Hospitals	Basic/Standard Care	Maximum Care Provided	Marketing
Applied principle	Focused offer with increasingly large numbers of cases while maintaining the same quality	Increasing numbers of cases while maintaining the same quality	Efficiency in quality through competition
Basis	Decreased patient beds, patient treatment days, and healthcare employers		
	Increased administration and numbers of patients/cases		

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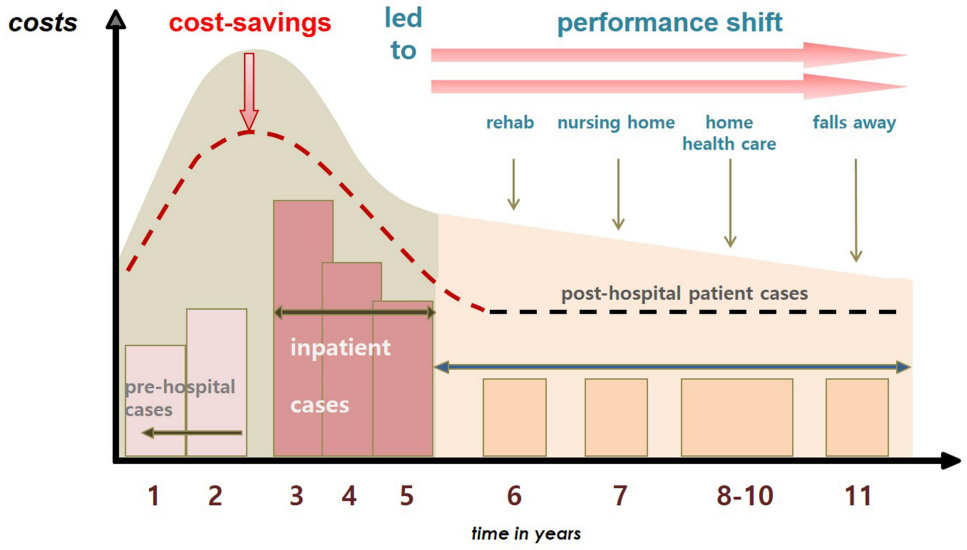

Figure 3 Decreased length of patient stay through the diagnosis-related group system resulted in a performance shift from inpatient cases to pre-hospital and post-hospital patient cases. The graph was modified according to the 2023 version, which was adapted with permission from Neubauer G. Ein Jahrzehnt Gesundheitsökonomie und Gesundheitspolitik 2000–2010, Band II. IfG, Institut für Gesundheitsökonomik, München, Deutschland; 2011.[74]

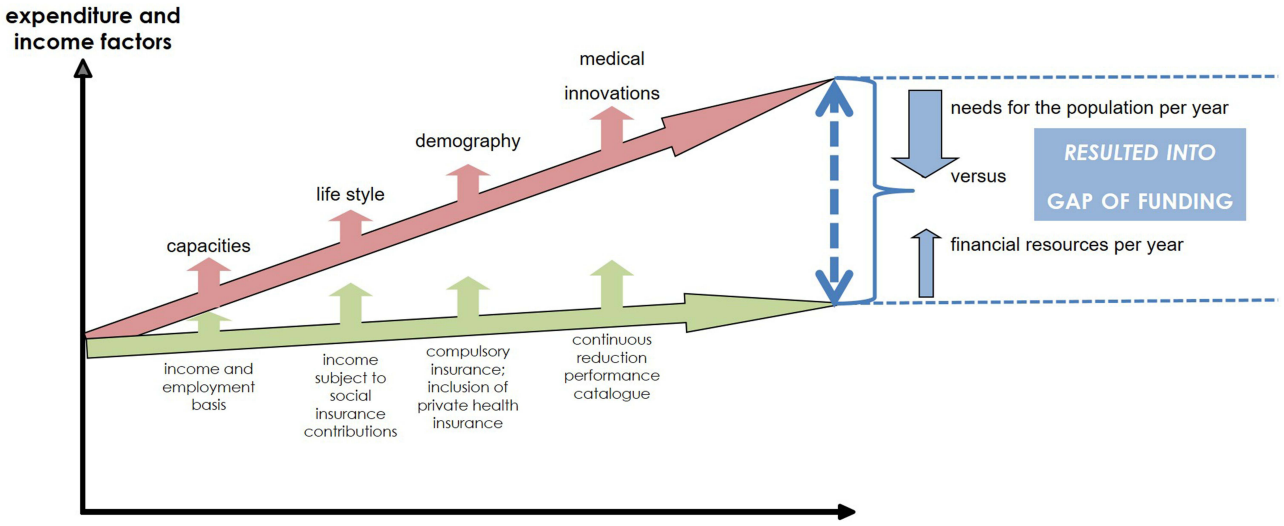

Figure 4 Continued lack of annual adjustment and consideration of stepwise variables resulted in a continued increase in the funding gap. The graph was modified in 2023, on the basis of a version from 2011 by the IfG, Institute for Health Economics. Adapted with permission from Neubauer G. Ein Jahrzehnt Gesundheitsökonomie und Gesundheitspolitik 2000–2010, Band II. IfG, Institut für Gesundheitsökonomik, München, Deutschland; 2011.[74]

savings to the surface, not only in Germany but also across the Western world, in accordance with a statement by Quintus Septimius Florens Tertullianus (Tertullian) (155 AD–220 AD): "Time brings everything to light!" (Latin: "Omnia tempus revelat!").[79] Even misperceptions of meta-analyses that such would always provide neat and concise conclusions, have been unmasked.[80]

Interdisciplinarity in healthcare and science involves substantial natural tension (Figure 6).[81] Daily interdisciplinary challenges are encountered, in combining clinical disease and in research in basic and translational sciences. Each involves effort and money. Quantity focus, explained by the derogatory term "medical tourism" alone has built

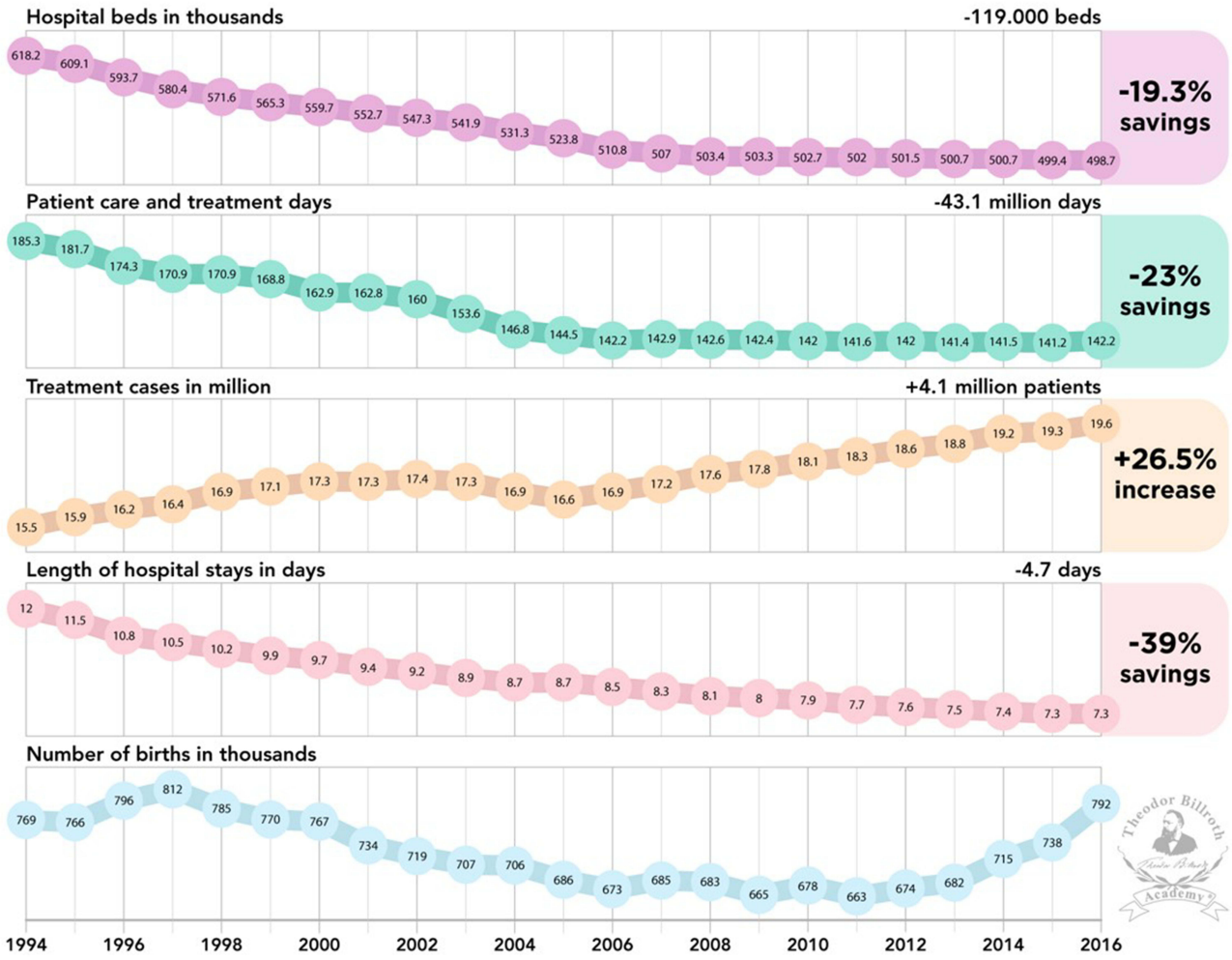

Figure 5 Graph originally published in 2019.[73] representing changes in hospital beds in thousands, patient care treatment days, treated cases in millions, length of hospital stays in days, and number of births in thousands in Germany, during a 22-year time period between 1994 and 2016. The data and the graph were modified and updated from a 2011 version by IfG, Institute for Health Economics.[74]

a multibillion-dollar market,[82] and led to consequences such as organ trafficking, transplantation tourism, or even loss of domestic spending or stem cell tourism.[83,84] In reality, these outcomes are based on quantity focus in monetary terms.

How is technology applied to this?

Technology

Technology is free of moral considerations, which are a concern of humans but not of technology itself. The economic definition of biotechnology is as follows:

> The application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.[85]

Biotechnology is already a subset of the bioeconomy, defined as follows:

> The bioeconomy covers all sectors and systems that rely on biological resources (animals, plants, micro-organisms, and derived biomass, including organic waste), their functions and principles.[86]

The market volume of data businesses in 2023 was $77 billion, and is expected to grow to $103 billion by 2027.[87] The global biomarker market alone is estimated to reach $194.21 billion by 2023, including a 13.6% increase in India

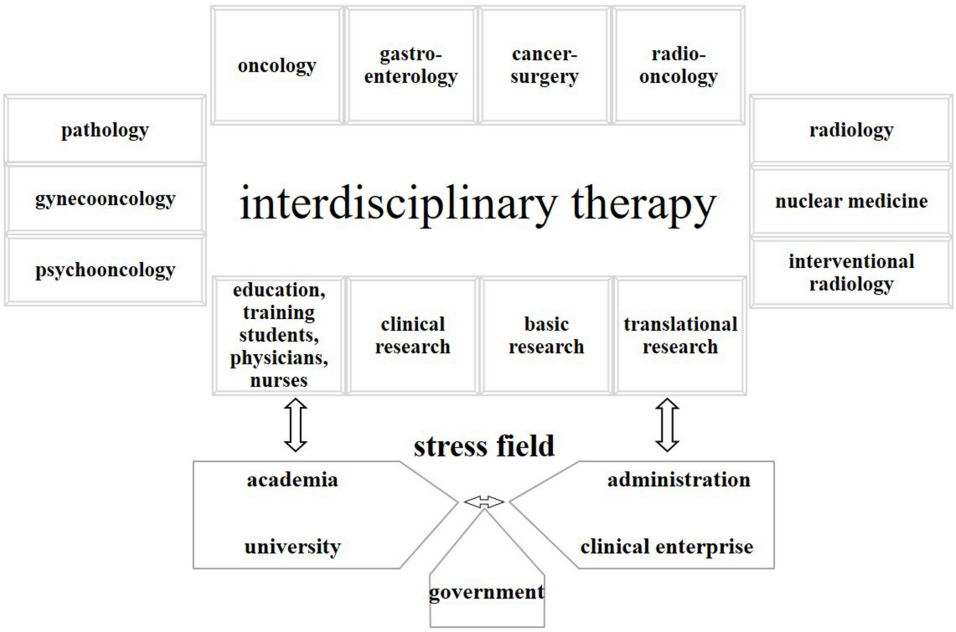

Figure 6 Tension field of interdisciplinary tumor board work-up, including interactions with academia, university, administration, clinical enterprise, and governmental regulation. Reprinted with permission from Brücher BLDM, Itzhak A, Bilchik A, et al. Carcinomatosis: cytoreduction and Heated Intraperitoneal Chemotherapy (HIPEC) Versus Palliation. In: Steele SR, Maykel JA, Champagne BJ, Orangio GR, editors. Complexities in Colorectal Surgery: Decision-Making and Management. *Springer New York*. 2014:63–89. Springer Nature.[81]

alone between 2024 and 2030;[88] however, survival, mortality, relapse, and prevention have not been substantially influenced to date. Thus, academic technology transfer can be considered the commercialization of knowledge.[89,90]

As the commercialization of science advances, the focus on quantity in publishing increases, at the cost of quality.

Publishing

Clarence Marsh Case (1874–1946), in 1928, discussed the quality of American sociology in an article on scholarship in sociology, and coined the expression "publish or perish".[91] The impact factor is a measure of prestige but not of excellence.[92]

Logical consequences of a quantitative focus have emerged: the number of academic journals in 2020 was 46,736, and more than 5.14 million academic articles were published in 2022 with a 5-year growth rate of 22.7%.[93] The numbers of published articles have been assumed to be too high and to be harmful to the quality of science.[94,95] Currently, the number of published articles increases each day by approximately 3000, thus resulting in > 1 million articles per year,[96] which reaches a level of inflation in the sciences.[92]

The top five publishers comprise 10,254 journals making about some 20%,[97] and article processing charges provided a 2015–2018 revenue exceeding $1 billion.[98] The MDPI revenue in 2020 was between $190 and $230 million,[99] compared with $584.5 million for Springer in 2021.[100] The global publishing industry revenue was $76.3 billion in 2022 in 28 countries,[101] and the estimated annual revenue for the global academic publishing market exceeded US $25 billion and continues to increase.[102]

Another effect of the commercialization of publishing is citation silencing regarding former knowledge, as previously described.[65] Many examples exist in medicine and science. Thermistocles Gluck (1853–1942) performed animal experiments with successful liver resections in cats in 1882 and 1883.[103] Hugo Rex (1861–1936), in 1888, reported the classification of the liver according to the blood supply,[104] 10 years before James Cantile (1851–1926) from Scotland reported a classification in 1898,[105] and more than 60 years before the currently used Couinaud classification was reported 1952 by Claude Couinaud (1922–2008).[106] However, few current studies cite Rex or Cantile. Presenting others' work as one's own should not ethically be tolerated,[107] yet this notion is considered quaint.[92]

However, scientific content is distributed 24/7, thus resulting in incessant bombardment with largely poor-quality research.

Marketing and Media

Marketing with constant touting of achievements influences perceptions, convictions, beliefs, and decision-making, as well as strategy creation, funding organizations, and political decision-making regarding the allocation of research funds. Internet advertising is a business model.[108] Currently, 5.44 billion internet users and 5.07 billion social media users exist, representing 63.5% of the total global population, equating to 59.3%, with an annual increase of 4.2% and an increased overlap of social media platform users between approximately 30% and 52%.[109–111] The total potential reach of the advertising audience monthly is 2.93 billion users on Facebook, 2.51 billion users on YouTube, 2.39 billion users on Instagram, 945.2 million users on TikTok, 975.9 million users on Facebook Messenger, 857.1 million users on LinkedIn, and 544.5 million users on X.[111]

The relationship of postings can be seen as their relationship, and likes appear to represent the craving of both users and distributors for acceptance.[112] Articles highly tweeted about are 11 times more likely to later be highly cited.[113] Otherwise, social media starts to be seen as an intermediary making scientific content visible.[114] The resulting preferences influence social and individual life, as well as created values, political habits, and cultural norms.[115] However, serious concerns exist that social media platforms are unwilling to provide researchers with data to assess whether such platforms improve society.[116] Approximately 91% of respondents in a survey still believe that science drives innovation, and when people hear the word "science", they feel hopeful.[117] However, important questions pertain not only to dissemination of science but also to the implications of whether social media improve societies,[114] because social media are already powerful tools.[118] Persistent, repeated spreading of content results in an illusory truth effect, such that readers believe that the content is true.[119–121] This phenomenon is reproducible: when the spread of false information occurs, the false information gains acceptance, particularly if it is disseminated repeatedly.[122]

Societies are aware of "fake news",[123] which increasingly affects people's judgments regarding politics, as predatory publisher affecting healthcare and science.

Predatory Publishers

Predatory publishers can be considered a logical consequence of the multi-billion-dollar publishing machine,[124] in parallel with fabricated papers[125–127] and so-called paper mills[128] undermining scientific integrity. Paper mills are systematic "profit oriented, unofficial and potentially illegal organizations that produce and sell fraudulent manuscripts that seem to resemble genuine research".[129] Scientific fraud is widespread in academia but is rarely reported.[130] In addition, approximately 60% of the 2018 misconduct findings involved image manipulation.[131] but also incorrect nucleotide sequences or agents were identified.[132,133]

Increasing numbers of independent scientists defend scientific conscience and integrity. Examples include Leonid Schneider, Elisabeth Bik (@MicrobiomDigest), Adam Marcus (@amarcus), Stuart Richie (@StuartJRichie), Anna Abalkina (@AlbakinaAnna), Dorothy Bishop (@deevybee), Kaoru Sakabe (@KaoruSakabe), James Heathers (jameshealthers), and those with X pseudonyms, Smut Clyde (@SmutClyde), Morty (@mortenoxe), Cheshire (thatsrerettab1), Tiger (@TigerBB8), Mu Yang (@mumumouse2), Sci_Spy (@spy_sci), WiseWoman (@WeWuWiWo), LymeScience (@LymeScience), David Sanders (@DavidSandersRep), James Heaters (@jamesheathers), Jennifer Byrne (@JAByrneSci), and PSBrookes (@PSBrookes). Any threat to scientific integrity is a critical concern.[77,134] Fraud is increasingly detected,[133,135–141] but paper mills are not country specific,[142] and have been called cartel-like organizations.[143] However, a recent fact-check has indicated that even most popular science books are not peer-reviewed.[144]

The application of artificial intelligence (AI) in the era of digitization cannot be overlooked.[127] Many scientists are concerned that future AI tools will expand the problems of paper mills, fake science, fake reviews, and fake illustrations, given that more professionalized manipulation may be more difficult to detect.

The technological aspects of psychology and sociology aid in understanding influences on perception.

Perception: Psychologic and Sociologic Aspects

Psychology and the perception of how media content is spread and interpreted are crucial in the formation of opinions and beliefs.[145,146] Our daily media are flooded in banalized form by so-called chauffeur knowledge, which is challenging to differentiate from real knowledge.[147] Chauffeur knowledge dates to 1919 and relates to Klaus Schulz, the chauffeur of Max Planck (1858–1947). Schulz often listened to Planck's lectures and he suggested to give his lecture on quantum mechanics in Munich; the Nobel laureate from 1918 agreed, because the journey was fun for both men. Discriminating fiction from reality requires an investment of time, thought, and hard work.

This principle also applies to the increased spread of populistic views, which purposely trigger emotions such as uncertainty or fear.[148] A turning point regarding such psychological distress occurred in the COVID-19 pandemic, "from repeated media exposure to the outbreak". People have heightened susceptibility to misinformation when they are frightened and doubtful,[122,149] and headlines that dramatize and emotionalize consumers receive more attention than neutral headlines.[146] Currently, applied psychology is consistently and aggressively used in media during pre-election campaigns.[150,151] Whether anti-populism or moralism is sufficient against populism[152,153] is a moot question. Self-serving attribution bias describes people's willingness to cast themselves in a favorable light[154–156] German sociologist Maximilian Carl Emil Weber (1864–1920) defined power as "any chance of opposing one's will against reluctance within a social relationship, as well as what that opportunity is based on".[157,158]

Social psychology can aid in understanding why inappropriate marketing occurs, and different cultural habits appear to exist in this regard. The citizens of some countries, eg, the US, tend to attribute people's behaviors to their personalities (correspondence distortion), whereas those in other countries, eg, South Korea, tend to attribute human behavior to situations.[159] In a 2004 survey, Ghanaian industrial workers often cited external circumstances as causes of work-related accidents, whereas their supervisors attributed the accidents to the workers themselves, thus suggesting a self-protecting bias.[159,160] In a meta-analysis of 266 studies, self-serving attributional biases were found primarily in the US, Canada, Oceania, Africa, Eastern Europe, and Russia, and showed high variability across ages, cultures, and psychopathology. The extent of self-serving distortion within the US does not differ by ethnicity (eg, European, Asian, African, Hispanic, and Indian); however, in Asian cultures (eg, Pacific Islander and Indian), this distortion is (until today) rare or non-existent.[159,161]

Different cultures do not equally define, explain, and present behavior, successes, and failures, each of which is based on individual self-serving attribution bias. Corruption may be as old as human history, and started as early to interact in science, journals, institutions, or countries.[157,158,162] and can be defined as "a corrupt act violates responsibility toward at least one system of public or civic order and is in fact incompatible with (destructive of) any such system".[163,164] However, misconduct in science is a form of corruption and might not be a solely cultural trend; it is attributable to a drive for recognition and fame, as part of a more global phenomenon. Silence is tantamount to supporting corruption and harming others. This aspect may explain another paradox in science, in which top-ranked articles that have not been replicated are nonetheless frequently cited.[165] John Emerich Edward Dalberg-Acton, 1st Baron Acton (1834–1902), in a letter in 1887, wrote that "power tends to corrupt, and absolute power corrupts absolutely".[166] The distinction between the subjective terms of justice and injustice increasingly disappears,[167] including in the context of science.

Independently of ongoing marketing, the spread of information, and related psychology or sociology, the actual gains in the sciences have been much smaller than proposed.[168] An analysis of 25 million articles (1945–2010) in Web of Science and 3.9 million patents (1976–2010) in the US Patent and Trademark Office's Patents View database has concluded that "science and technology are becoming less disruptive", although the sheer numbers remained stable.

Discussion

Trend towards managerialism with a focus on quantity in health care and science endangers their integrity. Nevertheless, it remains the task of the foundations of actions in healthcare and science to make unavailable knowledge available to society and the individual – even if it is unpleasant. The necessary information about cancer, as an example, quantity focus of healthcare, technology, publishing, marketing and media, predatory publishers, followed by psychologic and sociologic aspects which influence our perception, were each provided.

Cancer costs increased by 292% during a 16-year period in the US, from $71.1 billion in 2004 to $207.7 billion in 2020, and are expected to rise to $245.6 billion by 2030;[169–171] costs for hematologic cancers increased costs itself by 10% in 2015, and the highest cost increase was 27% for leukemias, representing $2.35 billion. The costs of 29 cancers in 204 countries and territories from 2020 to 2050 have been estimated to be $25.2 trillion.[172] A hospital-based observational cost analysis has demonstrated that these costs are associated primarily with rising costs of radiotherapy (+161%) and chemotherapy (+137%), but not cancer surgery,[173] although complex cancer surgery increases. The global biotechnology market in 2023 was $1.55 trillion, and the annual growth rate was nearly 14% until 2030; moreover, the revenue in 2021 from Moderna, Pfizer/BioNTech, and Johnson & Johnson vaccines alone was $31 billion.[174] Overall, oncology therapy for very advanced cancer is not associated with improved survival.[175]

In parallel, the US Food and Drug Administration (FDA) budget for fiscal year 2019 was $5.7 billion, approximately 42% of which was paid by industry user fees.[176] The Priority Review and Accelerated Approval by the FDA Modernization Act (FDAMA) was followed by the introduction of the Fast Track designation in 1997.[177] The FDA triggered use of the term "breakthrough therapy designation",[178–180] thus implying the existence of a near cure, and/or directly or indirectly suggesting a precursor to innovation. Detailed strategies for "hastening oncology drug development while maintaining high-efficacy standards" were promoted[181] and supported.[182] Pharmaceutical interest increased "when federal regulators started giving certain drugs 'breakthrough' status",[183] although many trials lack medical evidence.[184] "Hidden conflicts" in FDA panels reviewing company drugs influence this situation.[185] Although multiple cancer drugs have received "breakthrough therapy" designation, none to date have been safer, more effective, or more novel than drugs without this designation.[186] Theodor Billroth, on September 20, 1890, stated that "the incidental, the representation, is lifted up by artisanal drilled lack of talent to the main thing, to artwork."[187] An unanswered question is whether hidden conflicts amount to corruption. If cancer therapy results in an increase in disease-free survival but not in overall survival and/or increased quality of life, does this make any sense? Only approximately 15% of drugs newly approved by the FDA[188] and by the European Medicines Agency (EMA)[189] show real survival benefits in follow-up trials. Claims that these drugs are "magic bullets" have not been realized. This may explain why trust in science decreased from 40% in 2020 to 29% in 2022.[190] The FDA is of course in a dilemma, when paradoxical transformation in healthcare and science are in use, eg when wrong assumptions on the origin of cancer and/or in the interpretation of earlier findings and/or non-specific reading, became independent, eg the SMT is consistently declared to be the origin of cancer, but in reality, it has only been proven for 5%, whereas the majority (80%) of cancers are still termed as "sporadic", meaning that their cause is unknown.[65]

Overall, five types of cancer (trachea-bronchus-lung cancer, CRC, breast cancer, liver cancer, and leukemia) will account for roughly half of cancer costs. A total of 80.5% of cancers are epithelial, and account for more than three-quarters of the costs, although, despite subanalyses, the overall relapse or mortality rates for epithelial cancers have not substantially changed in several decades. Additionally, overall cancer incidence rates continue to rise, particularly among young adults. Game-changer therapies have significance in advancing knowledge of cancer biology, yet real-world data have shown no marked improvements in the global incidence of cancer, patient survival, and cancer mortality or relapse, despite subanalyses of small subpopulations.

An ongoing paradoxon can also be recognized in the use eg of the germ cell theory out of which the cancer stem cell (CSC) hypothesis developed. Johannes Peter Müller (1801–1858), the teacher of Rudolf Ludwig Karl Virchow (1821–1902), had proposed in 1838, that cancer may derive from germinal nuclei (German: Keimzellen), but Müller was a very differentiated and precise pathologist. Contrary to the mass of allegations in the scientific literature, Müller had clearly not the opinion, that all cancers would derive from germinal nuclei[191]

> By the way, I am far from believing that all cell balls of carcinoma reticulare and simplex arise in this way as germ cells in other cells […] the phenomenon is not constant enough for that.

In the following,Julius Friedrich Cohnheim (1839–1884) had a different opinion about cancer development, and contrary to his teacher Virchow, he propagated the "germ cell dissociation theory": "Error, an irregularity in the embryonic structure in which the cause of the later tumor must be sought"[192] Cohnheim's germ dispersal theory developed into the cancer stem cell (CSC) hypothesis, which today is held only responsible for up to 1% of malignant tumors.

CD34+ and CD38- colony forming progenitors were identified as leukemia initiating cells in the peripheral blood of acute myeloid leukaemia (AML) patients,[193] and in immunodeficient mice, such leukemic blasts, were exclusively CD34 ++ CD38-.[194] Pediatric brain tumors contain neural stem-like cells,[195] and breast cancer analysis showed CD44+ and CD24- lineage to result in tumor growth in mice,[196] and isolation of CD133 stem cells in medulloblastoma in children and glioblastoma in adults were cultivated in 2003.[197] Injection of such into the brain in animal models resulted in growth of medulloblastomas and glioblastomas,[198] and this all directly resulted into the assumption, the CSC would be correct and proven. However, cancer stem cells adapt and proliferate when grown in different species,[199] and even the frequency of CSC are not important,[200] which was supported by the fact, that randomly chosen single cells in mouse lung and breast cancer cell lines form tumors following allografting histocompatible mice.[201] Both examples, the SMT and the CSC, can serve as parade examples, how paradoxical transformation occurred by misinterpretation.

Publication of scientific results is a necessary prerequisite for achieving trust and integrity in science,[74] but approximately 50% of a pool of approximately 400,000 scientists across 38 countries have been reported to quit science within a decade.[202,203] The rate of science faculty departures is also increasing,[204] and the recruitment of postdoctoral associates remains a struggle.[205] Only approximately 10% of PhDs and 17–21% of postdoctoral associates enter tenure-track faculty positions.[206–208] The absence of good role models within an atmosphere of trust and integrity may be underestimated as a contributing and important role model factor.[209] However, in reality, a global, even homemade, workforce crisis in healthcare is occurring,[210] as also occurs more broadly in science.[211] Currently, physicians and scientists are more interested in industry than academia,[212] but approximately 90% of startups fail, thus indicating that the efficiency of university demanded generating startups is extremely low.[213]

Conclusion

In contrast to the Humboldt Reform, the slogans today are different. However, the instrumentalization of the focus on quantity my managerialism used today endangers not just our foundations of actions in healthcare and science. Large investments in the Human Genome or Proteome Project have increased knowledge, yet have made less difference in overall survival, mortality, or relapse in the mass of cancers, epithelial cancers. The proposed vision of *Imagine a World without Cancer* remains therefore still utopic.[214] James Potter (1710–1776) has stated that "a fish rots from the head down",[215] a translation from Rumi's Third Book of Masnavi from 1270, which stated: "fish begins to stink at the head, not from the tail".[216] This statement may remind us and may reveal the greater focus on researching causative factors before symptomatic cancer research. The application of AI in healthcare and science is greatly hoped to be highly fruitful in making individual precision medicine much more effective for a wider research and patient research approach. Under this vision, AI is being massively advanced financially by many countries worldwide. Importantly, government and industry funding of research is primarily a business approach, not a scientific one per se, although it will have many positive effects in enriching healthcare and sciences. By now, it could be of help to accept and to stop to neglect that the mass of cancer development and growth is not induced by genetic mutations.[217,218] This aspect alone could re-focus research investment. "No fear of taboo subjects, otherwise it becomes ideological. Scientists must also address questions beyond the scientific and social mainstream".[219]

The integrity of healthcare and science is clearly being eroded. Monetary considerations thus potentially explaining the paradoxical transformation in which a focus on quality has been replaced by quantity. Awareness is necessary to re-focus on accountability, and move both healthcare and cancer research in a direction that will yield better results for patients.

Abbreviations

AI, artificial intelligence; CRC, colorectal cancer; EMA, European Medicines Agency; FDA, Food and Drug Administration; NCI, National Cancer Institute.

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